Heterotopic bone formation in abdominal incisions

Jonathan Charles MD Pathology*
John A Hunt MB BCh FRCS FRCS (Edin) Surgery**

Heterotopic bone formation in vertical abdominal wounds is a not infrequent and sometimes disabling complication of abdominal surgery, occurring predominantly in males. Excision of the bone is indicated only for marked discomfort or pain, usually produced by an active lifestyle. Under these circumstances, recurrence of bone following excision, would be highly undesirable and the prophylactic use of etidronate disodium may well be indicated to prevent new bone formation, as demonstrated by one of our cases (Case 8).

Introduction

Heterotopic bone formation in scars of abdominal incisions is not a rare occurrence, yet few reports are present in the literature[1-9]. We report 8 recent cases, all males, in one of whom the bone recurred after excision; in another, prophylactic treatment was given to prevent recurrence of bone formation in the surgical wound, using etidronate disodium (EHDP: Didronel). We present a review of the literature regarding heterotopic bone formation in abdominal wounds, indications for surgery and possible uses of EHDP.

Case reports

Case 1

A 53-year-old white male health professional underwent a subtotal gastrectomy for adenocarcinoma of the stomach, through a vertical incision. Two years later the patient died from metastatic disease. At autopsy, heterotopic bone formation was present in his abdominal scar.

Case 2

A 72-year-old retired white man underwent a partial colectomy for adenocarcinoma of the colon, through a vertical incision. Four months later bone formation was discovered in the scar and was surgically excised.

Case 3

A 45-year-old disabled white male laborer underwent vagotomy and pyloroplasty for intractable duodenal ulcer, through an upper midline incision. At the postoperative visit, induration was noted in the wound, which progressed to radiologically proven bone. His lifestyle was not hindered by the bone, which was thus left alone and has not changed in 3 years.

Case 4

A 69-year-old retired white man underwent palliative esophagectomy for advanced adenocarcinoma arising in Barrett's esophagus, through an upper midline and a separate right thoracic incision. Six weeks later bone 5 cm long was noted in the upper part of the vertical midline incision. This did not hinder him and was left alone.

Case 5

A 44-year-old white truck driver underwent a vagotomy, pyloroplasty and fundoplication for severe acid-pepsin disease, plus esophagitis. After several months, he was noted to have a piece of bone 3 x 2 cm in size at the upper end of his wound, near the xiphoid process. This did not progress nor interfere with his activities and was left alone.

Case 6

A 70-year-old retired white man underwent a high partial gastrectomy for gastric lymphoma. Two months later, in follow-up, he was noted to have a piece of bone about 5 cm long by 2-3 cm wide in the upper part of his abdominal scar. His main activity was walking and the bone did not hinder him, so it was left alone.

Case 7

A 40-year-old white laborer underwent drainage of a pancreatic pseudocyst through an upper midline incision. Bone formation was noted 3 weeks later in the scar. The bone was 10 cm long and bowed anteriorly, extending from xiphoid to umbilicus. As he became more active, it hindered his activities and was excised. The bone recurred but was only about 5 cm in length and no further surgery was performed.

Case 8

A 49-year-old white male plasterer underwent a cholecystectomy, appendectomy and repair of an umbilical hernia through an upper midline incision. Bone formation was noted 3 weeks later in the scar. The bone was large (6 x 4 x 3 cm), bowed forward, and continuous with the xiphoid process. The bone interfered mechanically with movement and was painful

(Continued on page 67) ➤

* Kauai Medical Group and Wilcox Memorial Hospital
Lihue, Hawaii
** Cabell Huntington Hospital, St Mary's Hospital and Marshall University School of Medicine
Huntington, West Virginia

Received for publication March 1, 1991.

ONLY ONE H_2-ANTAGONIST HEALS REFLUX ESOPHAGITIS AT DUODENAL ULCER DOSAGE. ONLY ONE.

Of all the H_2-receptor antagonists, only Axid heals and relieves reflux esophagitis at its standard duodenal ulcer dosage. Axid, **150** mg b.i.d., relieves heartburn in **86%** of patients after one day and **93%** after one week.[1]

AXID®
nizatidine
150 mg b.i.d.

ACID TESTED. PATIENT PROVEN.

1. Data on file, Lilly Research Laboratories.

See accompanying page for prescribing information.

NZ-2947-B-249304

HETEROTOPIC *(Continued from page 65)*

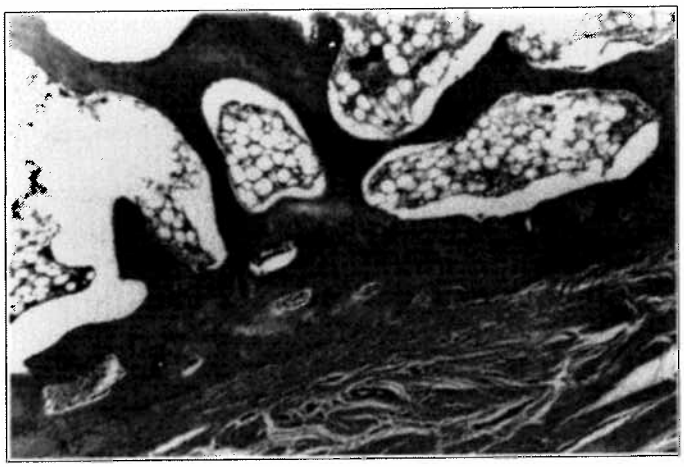

Figure 1: Case 8. Mature lamellar bone with sinuses containing fat and hematopoietic tissue, bordered by dense connective tissue. No cartilage is seen in this particular section. (Decalcified, paraffin-embedded, hematoxylin-eosin stain; magnification x40).

during his work as a plasterer. One month prior to its surgical excision, the patient was placed on a daily regimen of Didronel, 20 mg/kg/day. This dosage was continued for 3 months post-operation. There has been no recurrence of bone in the scar to date, 6 years following the excision.

The patients were of normal weight and not obese. They had no prior history of bone formation in other locations. In all cases the surgical incisions encroached upon the xiphoid process and the heterotopic bone later developed in the upper portions of the scar — in Cases 7 and 8 the heterotopic bone was actually attached to the xiphoid process. The bone varied in length from 3 cm to 10 cm. Otherwise, the scars were formed in a normal fashion.

The bone removed under these circumstances showed no histological difference from other forms of bone and contained lamellar bone, fat and hematopoietic tissue, with varying amounts of cartilage, all bordered by a rim of dense connective tissue. A microscopic section of the bone removed from Case 8 (Fig 1) together with an x-ray of the resected specimen is presented (Fig 2).

Discussion

Heterotopic bone formation in surgical wounds of the abdomen occurs only in longitudinal incisions (as opposed to horizontal ones)[1-8], thus implicating the xiphoid process or symphysis pubis as possible progenitors in its pathogenesis. The bone so formed is usually near to one of these structures, positioned between the anterior or posterior rectus sheath and the rectus abdominis muscle[3,5]. It presents itself anywhere from 3 weeks to several years following operations[2,5].

This bone formation has a distinct male preponderance[1,2,3,5], in that by 1962 only 5 of the 92 reported cases were in women[5]. This may be due in part to the fact that abdominal operations using longitudinal incisions are probably more common in males, considering the male predilection for peptic ulcer disease, carcinoma of the stomach, bladder and prostate. Abdominal operations in females, such as hysterectomies and Cesarean sections are frequently performed through low hori-

(Continued) ➤

Figure 2: Case 8. An x-ray of the specimen piece of bone resected from the patient who had been pre-tested with EHDP.

zontal incisions, while cholecystectomies are often performed through oblique transverse subcostal incisions, away from the costal margin. If bone did form in such incisions, it would very likely not inconvenience the patient, and may in fact not even be noticed.

There does not appear to be any evidence of a familial predisposition to this type of bone formation, though it has been reported in 2 brothers during the same time period[1].

There are basically 2 theories regarding the pathogenesis of heterotopic bone formation in surgical wounds[1-11]. One theory suggests that osteoblasts are derived through metaplasia of multi-potential mesenchymal cells already present in the fascia, or derived from granulation tissue. The second theory postulates that transposition of periosteal or perichondral fragments, disrupted at the time of surgery, will form a nidus for further bone growth. We do not see these processes as mutually exclusive and it is our belief that either of these modes of bone formation may occur, separately or together, keeping in mind that the linea alba is possibly a vestigial remnant of the sternum. There is no evidence linking heterotopic bone formation to any metabolic or endocrine disorder, nor to the nature of the suture material used[6].

The cure for heterotopic bone formation in surgical wounds has generally been surgical excision, with occasional postoperative radiation[6,8,9]. However, we now propose a possible preventive measure with the use of etidronate disodium (EHDP). EHDP is the only drug of its class of compounds — biphosphonates (formerly diphosphonates) — currently on the market. Biphosphonates are structural analogs of pyrophosphate, a naturally occurring inhibitor of bone formation. EHDP prevents the conversion of amorphous calcium phosphate to crystalline hydroxyapatite, the mineral component of bone. Furthermore, it also binds to the hydroxyapatite present, rendering it more resistant to chemical attack by alkaline and acid phosphatases produced by the osteoblasts and osteoclasts respectively[12,13]. It thus slows down both the dissolution and the accumulation of mineral. Also, it appears to interfere with the conversion of osteoblasts to osteocytes and markedly reduces the osteoclast population[12,13,14]. Serum calcium and parathyroid hormone levels are not significantly changed[14], yet in Paget's Disease a marked decrease in both urinary hydroxyproline and serum alkaline phosphatase is noted, reflecting decreased osteoclastic and osteoblastic activity[14-16]. In short, EHDP inhibits both bone remodeling and mineralization.

The principal use of EHDP is in the treatment of Paget's Disease[14-17]. It has also been recommended for heterotopic ossification in patients following severe head or spinal cord injury and following total hip arthroplasty[18,19,20]. EHDP has also been used with varying success in postmenopausal osteoporosis, myositis ossificans progressiva[21,22], calcinosis universalis[23], the prevention of periodontosis[24], and the prevention of calculi in the urinary tract[25]. On an investigational basis, it has been studied for the prevention of atherosclerosis[26]. Recently, the intravenous administration of dichloromethylene diphosphonate (not currently on the market) and EHDP have shown great promise in lowering the serum calcium in patients with hypercalcemia of malignancy[27,28].

The side effects of EHDP therapy are usually manifested only when large or prolonged doses are administered, consisting of gastrointestinal upsets[14,18], osteomalacia (with increased likelihood of pathologic fractures)[12,16,17], hyperphosphatemia[12,14], and an increase in bone pain[16,18].

Apart from its primary use in Paget's Disease, EHDP exerts its most beneficial effect in the prevention of heterotopic bone formation before its actual onset, rather than as treatment[18,20].

Two of our patients (Cases 7 and 8) experienced severe pain and inconvenience from the large ossified fragments in their abdominal wounds. Since in each patient the heterotopic bone was attached to the xiphoid process, there was considerable limitation of their activities as construction workers. It is known that trauma and heavy physical labor can predispose to heterotopic bone formation[2]. With these considerations in mind, and after the bone recurred in Case 7, the next patient (Case 8) received pre- and postoperative EHDP and has not had a recurrence of heterotopic bone formation after 6 years.

REFERENCES

1. Tama L: Heterotopic bone formation in abdominal surgical scars: a report of two cases in brothers. *JAMA* 1966,197(3):151-153.
2. Sanders RL: Bone formation in upper abdominal scars. *Ann Surg* 1955;141(5):621-626.
3. Classen KL, Wiederanders RE, Herrington JL Jr.: Heterotopic bone formation developing in abdominal scars. *Surg* 1960,47(6):918-923.
4. Watkins GL: Bone formation in abdominal scars after xiphoidectomy. *Arch Surg* 1964;89:731-734.
5. Lehrman A, Pratt, JH, Parkhill EM: Heterotopic bone in laparotomy scars. *Am J Surg* 1962;104-591-596.
6. Eidelman A, Waron M: Heterotopic ossification in abdominal operation scars. *Arch Surg* 1973;107:87-88.
7. Marteinsson BTH, Musgrove JE: Heterotopic bone formation in abdominal incisions. *Am J Surg* 1975,130:23-25.
8. Apostolidis NS, Legakis NC, Gregoriadis GC et al: Heterotopic bone formation in abdominal operation scars. Report of six cases with review of the literature. *Am J Surg* 1981, 142:555-559.
9. Spencer GR: Heterotopic bone formation in abdominal incisions. *JR Coll Surg Edinb* 1982,27(4):245-6.
10. Soren A, Waugh TR: The morphologic and pathogenetic bases of heterotopic bone formation in the extremities. *Zentralbl Allg Pathol* 1983,127:91-96.
11. Puzas JE, Miller MD, Rosier RN: Pathologic bone formation. *Clin Orthop Rel Res* 1989,245:269-281.
12. Heaney RP, Saville PD: Etidronate disodium in postmenopausal osteoporosis. *Clin Pharmacol Ther* 1976,20(5):593-604.
13. Plasmans CMT, Juypers W, Slooff TJJH: The effect of ethane-l-hydroxy-l, l-diphosphonic acid (EHDP) on matrix induced ectopic bone formation. *Clin Ortop* 1978,132:233-243.
14. Alexandre CM, Chaping MC, Vignon E et al: Treatment of Paget's disease of bone with ethane-l, hydroxy-1, 1-diphosphonate (EHDP) at a low dosage (5 mg/kg/day). *Clin Orthop* 1983,174:193-205.
15. Basle MF, Rebel A, Renier JC et al: Bone tissue in Paget's disease treated by ethane-l, hydroxy-1, 1-diphosphonate (EHDP). Structure, ultrastructure, and immunocytology. *Clin Orthop* 1984,184:281-288.
16. Krane SM: Etidronate disodium in the treatment of Paget's disease of bone. *Ann Intern Med* 1982,96(5):619-625.
17. Merkow RL, Lane JM: Current concepts of Paget's disease of bone. *Orthop Clin N Amer* 1984,15(4):747-763.
18. Garland DF, Alday B, Venos KG, Vogt JC: Diphosphonate treatment for heterotopic ossification in spinal cord injury patients. *Clin Orthop* 1983,176:197-200.
19. Thomas BJ, Amstutz HC: Results of the administration of diphosphonate for the prevention of heterotopic ossification after total hip arthroplasty. *J Bone Joint Surg* 1985,67A(3):400-403.
20. Spielman G, Gennarelli TA, Rogers CR: Disodium etidronate: its role in preventing heterotopic ossification in severe head injury. *Arch Phys Med Rehabil* 1983,64:539-542.
21. Elliott DF: Fibrodysplasia ossificans progressiva (FOP) treated with diphosphonate. *Birth Defects* 1974,10:515-520.
22. Smith R, Russell RGG, Woods CG: Myositis ossificans progressiva. *J Bone Joint Surg* 1976,58B:48-57.
23. Cram RL, Barmada R, Geho WB, Ray RD: Diphosphonate treatment of calcinosis universalis. *N Eng J Med* 1971,285:1012-1013.
24. Sturzenburger PO, Swancar JR, Reiter G: Reduction of dental calculus in humans through the use of a dentifrice containing a crystal-growth inhibitor. *J Periodontol* 1971,42:416-419.
25. Baumann JM, Ganz U, Bisaz S, Fleisch H, Rutishauer G: Verabreichung eines diphosphonates zur steinprophylaxe. *Helv Chir Acta* 1974,41:421424.
26. Wagner WD, Clarkson TB, Foster J: Contrasting effects of ethane-l, hydroxy-1, 1-diphosphonate (EHDP) on the regression of two types of dietary-induced atherosclerosis. *Atherosclerosis* 1977,27:419-435.
27. Singer FR: Role of the biphosphonate etidronate in the therapy of cancer-related hypercalcemia. *Sem Oncol* 1990,17(2):34-39.
28. Canfield RE (guest editor): Etridronate disodium: a new therapy for hypercalcemia of malignancy. *Am J Med* (Symposium) 1987,82(2A):1-78.

■